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Diagnostic value of un-enhanced MRI in differentiation of hemangioma and metastasis

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Abstract:
Objective: *To compare the role of un-enhanced MRI in the differentiation of hemangioma and metastasis.*
Materials and methods:*By performing a retrospective computerized search for all subjects who underwent liver in Medical Imaging center of Imam Khomeini hospital between February 2013 and April 2017, we identified 87 patients with hemangioma and metastasis (43 men and 44women;age, 18–86years; mean age 51.1 years). Patients were referred to this center for first assessment of ultrasound-detected liver lesions. None of patients received previous medical or interventional treatment of any nature. All patients with hemangioma and metastasis larger than 1.5 cm were included in the study. Patients with Immune deficiency, treated liver tumors were excluded from the study. Images analysis was done according to the difference in the signal intensity, site, shape, size of the lesions and their relations to the surrounding structures at the several sequences (T1-weighted, T2-weighted and heavily T2 pulse sequences) Then, we reviewed diffusion-weighted imaging (DWI) study with the b-value of 50,400 and 800 , ADC value measurements were performed by placing the regions of interest (ROIs) on ADC maps and carefully drawing manually to encompass the entire lesions, without necrotic cores if present. For lesions not easily identified on DWI, the locations were determined using T2-weighted images. The ROIs in the surrounding organ to avoided intrahepatic vessels and motion artifacts. The mean ADC value of each ADC was obtained.*
Results:*A total of 141 lesions in 87 patients were assessed. Mean age of patients was 51.1 years [18-86]. Among the patients, 44 were female [50.5%] and 43 were male [49.5%]. There was not any significant difference in the gender between hemangioma and metastasis (p value: 0.14). Among all lesions, 62 were metastasis [43.9%] and 79 were benign [56.1%]. Final diagnosis of all hemangioma were proved by follow up [100%] and all of metastasis were proved by biopsy [100%]*
Conclusion: *this study showed high efficacy of diffusion-weighted imaging compared to conventional MRI. Diffusion weighted imaging can reliably differentiate hemangioma from metastasis lesions. Diffusion weighted imaging should be implemented into routine imaging of hepatic lesions not characterized in other imaging modalities*
Key Words: *Liver, un-enhanced MRI, hemangioma, metastasis.*

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I. Introduction

The liver is considered a common site for many benign and metastatic focal lesions. Accurate diagnosis of these is important in oncological patients for an accurate staging and in patients without known oncological pathology for avoiding unnecessary liver biopsies.[1]

With the widespread use of imaging methods, the detection of focal hepatic lesions (FHLs) has become gradually familiar. But the detection of focal hepatic lesions does not constitute the main problem because of improved image quality with new generation of ultrasound (US) equipment's and multi-detector computed tomography's (MDCT). However, the differential characterization of benign and malignant focal hepatic lesions remains a diagnostic challenge. The difficulties are to classify these lesions as benign or malignant, to characterize them into subtypes. Currently, MRI has been used for this purpose but it has some difficulties such as vascular metastases may resemble hemangiomas during the imaging[2-4]. Several features of FHLs on computed tomography (CT) and magnetic resonance imaging (MRI) are useful for their characterization. CT and MRI rely on the use of contrast agents and multiphasic studies for evaluation of enhancement characteristics that provide valuable indications to FHL type. However, the use of contrast agents can be expensive and could be contraindicated in some patients; Long acquisition times in dynamic MRI could also prevent optimal evaluation[5]. Diffusion-weighted imaging (DWI) is a new MRI technique that provides imaging of water diffusion in biological tissues[6]. Since fast imaging sequences facilitated abdominal examinations and reduced the respiratory artifacts, the diagnostic utility of DW-MRI has been increased in abdominal examinations[7]. Herein, this study was done to diagnostic value of un-enhanced MRI in differentiation of hemangioma and metastatic lesions.

II. Materials and methods

Study design and patient selection

By performing a retrospective computerized search for all subjects who underwent liver MRI between February 2013 and April 2017, we identified 87 patients with hemangioma and metastasis (43 men and 44 women;age, 18–86 years; mean age 51.1 years). Patients were referred to this center for first assessment of ultrasound-detected liver lesions. None of patients received previous medical or interventional treatment of any nature. All patients with hemangioma and metastasis larger than 1.5 cm were included in the study. Patients with Immune deficiency, treated liver tumors were excluded from the study.

The institutional review board and local ethics committee at the university approved this study. Written informed consent was obtained from all participants after providing detailed description of the study method.

MRI protocol

Examinations were performed on a 3 T magnet (Magnetom Avanto, Siemens Medical Systems, Erlangen, Germany) using a surface phased-array body coil.

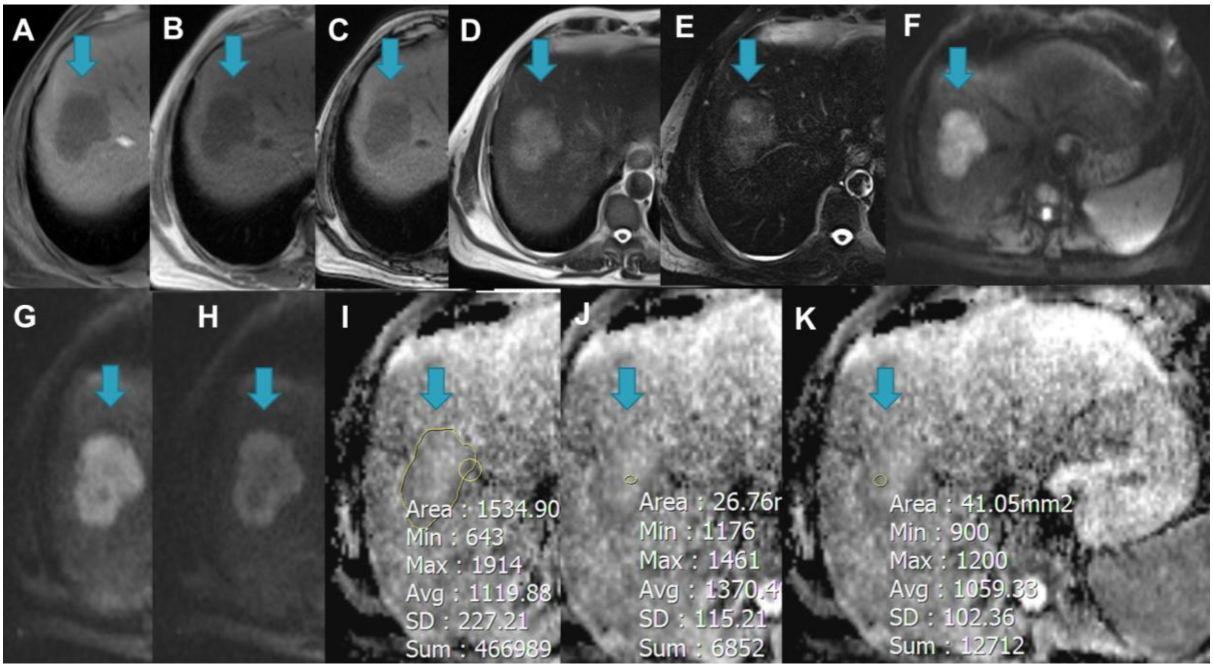
In our Institution, the MRI protocol for the upper abdomen includes multi-breath hold Gradient Echo (GE) in-phase and out of-phase T1-weighted imaging (TR 100 msec; TE 1.1/2.2 msec; FOV 300x400 mm; matrix 512x384; slice thickness 6 mm; number of slices 32; acquisition time 41 sec) and axial (eventually coronal) multi-breath hold Short Time Inversion Recovery (STIR) or respiratory-triggered Spectral Adiabatic Inversion Recovery (SPAIR) T2-weighted sequence (TR 3770/4510 msec; TE 134/65 msec; FOV 300x400/285x380 mm; matrix 512x384/320x240; slice thickness 6/6 mm; number of slices 30/30; nominal acquisition time 1.41 min/1.50 min). These sequences were followed by a dynamic study using a volumetric, fat-satured Volume Interpolated Breath Hold Examination (VIBE) T1-weighted volumetric sequence (TR 4.2 msec; TE 1.4 msec; FOV 337x400 mm; matrix 256x216; slice thickness 4 mm; number of slices 56; acquisition time of a single breath hold 11 sec) before and after intravenous injection of 0.1 mL/Kg of gadobenatedimeglumine (MultiHance, Bracco, Milan, Italy). The sequence was repeated on the axial plane after 30, 70 and 300 sec after contrast administration. Images were acquired also in the hepatospecific phase at about 1 hour after contrast administration.

DWI was performed before the dynamic study with a respiratory-triggered Single-Shot Echo-planar sequence acquired on the axial plane, with b values of 50, 400 and 800 sec/mm2 (TR 4400 msec; TE 76 msec; FOV 380x285 mm; matrix 115x192; slice thickness 6 mm; number of slices 24; flip angle 150 deg; technique and a parallel imaging algorithm (Generalized Autocalibrating Partially Parallel Acquisition; GRAPPA) with an acceleration factor of 2.

Image analysis

Images analysis was done according to the difference in the signal intensity, site, shape, size of the lesions and their relations to the surrounding structures at the several sequences (T1-weighted, T1 in and out phase, T2-weighted and heavily T2 pulse sequences) Then, we reviewed diffusion-weighted imaging (DWI) study with the b-value of 50,400 and 800 to assess the added diagnostic value in the detection and characterization of the hepatic focal lesions. On DWI, restricted diffusion was considered if a lesion showed increased signals to the normal liver parenchyma on high b-value images, and when the ADC (apparent diffusion coefficient) map displayed a value lower or equal to liver parenchyma. The readers visually evaluated the ADC map qualitatively, comparing to that of normal surrounding liver parenchyma. The bright signal on both diffusion images and ADC map are considered as T2 shine-through effect which was seen in hemangiomas and cysts.

ADC values for each lesion were measured by a single observer (H.J.T., with five years of experience in abdominal imaging), who was blinded to the clinical history, imaging reports, and pathologic results. ADC maps were obtained on the MR console using post-processing software. ADC value measurements were performed by placing the regions of interest (ROIs) on ADC maps and carefully drawing manually to encompass the entire lesions, without necrotic cores if present. For lesions not easily identified on DWI, the locations were determined using T2-weighted and/or contrast-enhanced T1-weighted images. The ROIs in the surrounding organ to avoided intrahepatic vessels and motion artifacts. The mean ADC value was obtained.(Fig1)



III. Data analysis

For analyzing statistical data, SPSS, t and chi-square method used. In all results, P value<0.05 considered as significant level. Diagnostic indices of MR imaging methods calculated based on sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios.

IV. Results

A total of 141 lesions in 87 patients were assessed. Mean age of patients was 51.1years [18-86]. Among the patients, 44 were female [50.5%] and 43 were male [49.5%]. There was not any significant difference in the gender between hemangioma and metastasis(p value: 0.14). Among all lesions, 62 were metastasis [43.9%] and 79 were benign [56.1%]. Final diagnosis of all hemangioma were proved by follow up [100%] and all of metastasis were proved by biopsy [100%]

Most of the hemangioma had markedly high signal on T2 sequence, while most of the metastasis lesions had mild to moderate T2 hyper-intensity. T2 signal difference was statistically significant in discrimination of hemangioma and metastatic lesions. (p<0.001). Most being lesions did not signal drop on heavy T2 sequence, while all malignant lesions had partial or complete signal drop out on heavy T2. (p value<0.001)

Diffusion weighted imaging was highly valuable in differentiation of hemangioma and metastasis lesions as 79 hemangioma showed hyper-intensity on ADC map, whereas all metastasis lesions showed hypo-intense ADC(restricted diffusion). ADC value was 98% accurate to differentiate between hemangioma and metastasis lesions.(Table1),(Table 2) shows the accuracy of each given cutoff point for discrimination of hemangioma and metastasis lesions.

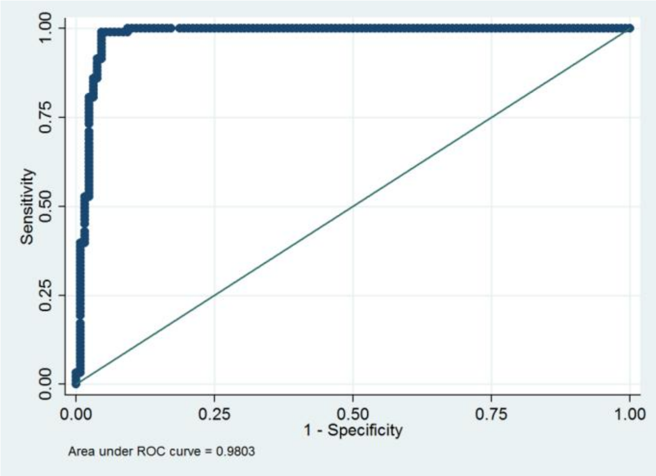
Table 1. The value of ADC signal for differentiation of hemangioma from metastatic lesions.

Index	*Symbol*	*Estimate*	*Lower 95% CI*	*Upper 95% CI*
Sensitivity	SE	1/0000	0/9611	#NUM!
Specificity	SP	0/9688	0/9219	0/9914
Efficiency (Correct classification rate)	EFF	0/9819	0/9543	0/9950
Predictive value of positive test	PVP	0/9588	0/8978	0/9887
Predictive value of negative test	PVN	1/0000	0/9707	#NUM!
Likelihood ratio of positive test	LR+	32/0000	12/1970	83/9553
Likelihood ratio of negative test	LR-	#DIV/0!	#DIV/0!	#DIV/0!
Cohen’s Kappa	K	0/9631	0/9273	0/9989

Table 2. The accuracy of various cutoff points of ADC for differentiation of benign and malignant lesions

Variable	Cutoff	Sen. [95% CI]	Spec. [95% CI]	PPV [95% CI]	NPV [95% CI]	PLR [95% CI]	NLR [95% CI]	Efficacy [95% CI]
ADC Mean	**≤0.49**	0.03 [0.01-0.09]	1 [0.97-1]	1 [0.29-1]	0.59 [0.52-0.65]	------	1.03 [0.99-1.07]	0.59 [0.52-0.65]
	≤0.8	0.41 [0.31-0.52]	0.98 [0.94-0.99]	0.95 [0.83-0.99]	0.70 [0.62-0.76]	26.2 [6.5-105.6]	1.7 [1.4-2]	0.74 [0.68-0.80]
	≤1.4	1 [0.96-0.1]	0.88 [0.81-0.93]	0.85 [0.77-0.91]	1 [0.97-1]	8 [5.1-12.7]	--------	0.93 [0.89-0.96]

Fig 2. ROC curve for ADC part mean.



V. Discussion

Differentiation of benign and malignant hepatic lesions have been always challenging for radiologists. Various imaging methods exists for this purpose, however no single imaging modality might be enough for proper discrimination of liver lesions. This study assessed the diagnostic value of un-enhanced MRI in differentiation of hemangioma and metastasis hepatic lesions.

Diffusion weighted imaging has emerged as a non-invasive tool in assessment of these lesions. DWI is a measure of random Brownian motion of free water molecules in a given environment. Most commonly, diffusion weighted imaging is performed by adding two motion-sensitive gradient pulses to either sides of a 180 refocusing pulse in a T2 spin echo sequence. The first gradient creates a phase shift which is controlled by the gradient strength at the position of each spin. Then during the second gradient pulse, non-mobile (restricted) spins will experience the same gradient strength and will rephrase to their stationary positions, but mobile spins will experience a different gradient strength and will go on a total phase shift, not returning to their initial locations. This will cause signal loss for mobile spins. To obtain highly sensitive Diffusion weighted images, the amplitude and duration of two gradients should be increased. These gradient features are generally known as b value. After taking diffusion images, ADC map is drawn by deducting signal of diffusion images with two different b values[4].

Diffusion weighted imaging is shown to be reliable for recognition of liver metastases. An accuracy of 97% is reported for diffusion weighted imaging to detect metastasis compared to 78% accuracy of CT scan.. In a study by Bruegel and Rummeny[8], DWI had higher sensitivity than T2-weighted sequence and comparable specificity with superparamagnetic iron oxide (SPIO) or gadolinium-enhanced MR imaging for the recognition of hepatic metastases[9]. Distinction the benign from malignant hepatic lesions is a common diagnostic difficulty at magnetic resonance (MR) imaging. This distinction has significant treatment consequences in people who have or are suspected of having cancer or in people with lesions recognized incidentally at screening MR imaging. [10]Various studies have reported that DWI has the possibility to distinguish benign and malignant focal hepatic lesions[11-13]. Nevertheless, this has been challenged[11, 13]. According to the study of Badawy et all[14], ADC value can provide a quantitative measure of lesion diffusion without the requirement for contrast agent.Elbarbary et all [15]found the lowest ADCs in metastases, hepatocellular carcinoma and cholangiocarcinoma. A significant difference was found between the mean ADC values of benign and malignant lesions. The differences in ADC values among various benign lesions or various malignant lesions were not significant.Tesla et al showed ADC values to be useful in the differentiation between metastasis and benign solid hepatic lesions. However, the exclusion of cysts in the analysis revealed to a lower cut off value and lower accuracy than previously mentioned.In a study conducted by Rio et al., 51 Solid mass in the liver of 26 patients were examined by MRI. Their results showed that the ADC 1.28 * 10^{-3} mm2 / sec cut off for differentiating benign from malignant hepatic tumors. ADC of benign from malignant neoplasms was significantly more. Highest ADC value was seen with hemangioma, while lowest values belonged to metastasis. [16]In the study by Kim et al, 6 healthy subjects,30 benign and 49 malignant tumors were evlauted. Their results showed that that benign lesion have significantly higher ADC values[17].

We found high accuracy of ADC value for differentiation of hemangioma and metastasis liver lesions. Several conventional MRI indices such as T2 signal and signal drop out on heavily T2 sequences were useful as well; however there was considerable overlap between the results.

This study was subject to several limitations. First, tissue diagnosis was not available in a large subset of patients and the diagnosis was based on follow-up. Second, thenumber of certain subtypes of liver lesions was low and definite behavior of these lesions on MR imaging might not be concluded form this data.

In conclusion, this study showed high efficacy of diffusion-weighted imaging compared to conventional MRI. Diffusion weighted imaging can reliably differentiate hemangioma from metastasis lesions. Diffusion weighted imaging should be implemented into routine imaging of hepatic lesions not characterized in other imaging modalities.

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